REMARKS

The Office Action states that should claim 44 be found allowable, claim 51 will be objected to under 37 C.F.R. 1.75 as being a substantial duplicate thereof. Claim 51 has been canceled without prejudice or disclaimer, and the objection is now moot.

Claim 56 stands rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. Specifically, the Office Action alleges that the limitation "about 10 nM" is not supported by the specification. To expedite prosecution, and without admitting or commenting on the propriety of the rejection, the Applicants have amended Claim 56 to replace the phrase "about 10 nM" with the phrase "10 nM." The Applicants respectfully submit that the grounds of the rejection have been obviated and withdrawal of the rejection under 35 U.S.C. §112, first paragraph, is respectfully requested.

Claims 43 and 45-47 stand rejected under 35 U.S.C. §102(e) as being anticipated by Lisziewicz et al. (hereinafter "Lisziewicz'). Claims 43 and 45-47 further stand rejected under 35 U.S.C. §102(b) as being anticipated by Buseyne et al. (hereinafter "Buseyne").

A claim is anticipated only if each and every element as set forth in the claim is found in a single prior art reference. The identical subject matter must be shown in as complete detail as is contained in the claim. There must be no difference between the claimed subject matter and the reference disclosure, as viewed by a person of ordinary skill in the art.

In this case, independent claim 43 is directed to a pharmaceutical composition comprising: a therapeutically effective amount of an antigen presenting cell pulsed with an inactivated non-recombinant human immunodeficiency virus (HIV); and a pharmaceutically acceptable carrier; wherein the inactivated human immunodeficiency virus is **chemically**

inactivated by 2,2'-dithiopyridine, and wherein the composition expands *in vivo* expression of virus-specific CD8+T cells, and said virus-specific CD8+ cells kill HIV-infected cells.

In contrast, Lisziewicz generally describes a composition comprising an antigen presenting cell pulsed with an **heat**-inactivated HIV. The rejection asserts that Lisziewicz teaches the claimed invention because the product of interest is inactivated HIV and Lisziewicz teaches this product (The Office Action, page 6).

In sharp contrast, Claim 43 recites "wherein the inactivated human immunodeficiency virus is **chemically** inactivated by 2,2'-dithiopyridine." It is well known in the art that chemical 2,2'-dithiopyridine (AT-2) inactivation differs from heat-inactivation in which the AT-2 inactivation preserves the intact native conformation of virus proteins. The Applicants enclose for the Examiner's convenience Fantuzzi et al., *J. Immunol.*, 5381-5387 (2001) which describes that, in contrast to conventional methods of inactivation (i.e., heat or formalin treatment), AT-2 inactivation allows viruses to retain conformational and functional integrity of viral surface proteins. Thus, the heat-inactivated HIV in Lisziewicz is different from the AT-2 inactivated HIV in Claim 43.

Therefore, Lisziewicz does not anticipate independent claim 43 since Lisziewicz does not disclose every and each element recited in claim 43. Claims 45-47 are not anticipate by Lisziewicz since they depend from claim 43 and recite additional elements. Withdrawal of the rejection based on Lisziewicz is respectfully requested.

Buseyne generally describes that exposure of dendritic cells to AT-2 inactivated HIV strain induces IFN-γ production. The experiment described in the Buseyne was carried out in an *in vitro* setting. Buseyne does not teach or suggest "a pharmaceutical composition comprising a therapeutically effective amount of an antigen presenting cell pulsed with an inactivated non-

recombinant human immunodeficiency virus (HIV); and a pharmaceutically acceptable carrier," as recited in Claim 43. Buseyne does not anticipate Claim 43 because Buseyne does not disclose every element of Claim 43. Applicants further submit that claims 45-47 are patentable over Buseyne because they depend from Claim 43 and recite additional patentable subject matter. Moreover, Buseyne used HIV strain MN. This HIV strain is not considered to be autologous; see, e.g., Nokta et al. (1996), AIDS Weekly via NewsRx.com, "Neutralization profile of sera from HIV infected patients to autologous HIV isolates and MN Strain," a copy of which is enclosed for the Examiner's convenience. Claim 44 recites an autologous HIV strain. The method of claim 44 is also not anticipated by Busyene because it discloses a non-autologous HIV strain.

Withdrawal of the rejection based on Busyene is respectfully requested.

Claims 52-56 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Buseyne in view of Lu et al. (hereinafter "Lu"). Claims 44 and 51 stand rejected under 35 U.S.C. §103(a) being unpatentable over Buseyne in view of Lieberman et al. (hereinafter "Lieberman").

To establish a prima facie case of obviousness, all the claim limitations must be suggested by the prior art. Furthermore, when applying 35 U.S.C. §103, the Patent Office is required to adhere to the following: (1) The claimed subject matter must be considered as a whole; (2) The references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination; (3) The references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed subject matter; and (4) Reasonable expectation of success is the standard with which obviousness is determined.

As described above, claims 43 and 44 are directed to a pharmaceutical composition comprising: a therapeutically effective amount of an antigen presenting cell pulsed with an

inactivated non-recombinant human immunodeficiency virus (HIV); and a pharmaceutically acceptable carrier; wherein the inactivated human immunodeficiency virus is chemically inactivated by 2,2'-dithiopyridine, and wherein the composition expands *in vivo* expression of virus-specific CD8+T cells, and said virus-specific CD8+ cells kill HIV-infected cells.

In sharp contrast, Buseyne only generally describes that exposure of dendritic cells to AT-2 inactivated HIV strain induces IFN-γ production. The experiment described in Buseyne was carried out in an *in vitro* setting. Buseyne neither provides any *in vivo* data nor mentions "a pharmaceutical composition comprising a therapeutically effective amount of an antigen presenting cell pulsed with an inactivated non-recombinant human immunodeficiency virus (HIV); and a pharmaceutically acceptable carrier," as recited in claim 43 or 44 . Accordingly, Buseyne is not applicable to Claims 43 and 44 since Buseyne does not teach or suggest all the limitations recited in these claims.

Lu generally discloses that indinavir restores impaired T-cell proliferative response *in vivo* and *in vitro*. The rejection turns to Lu for its teachings on the effect of indinavir. However, the goal of Lu is to induce an anti-retroviral effect. Lu also does not disclose "a pharmaceutical composition comprising a therapeutically effective amount of an antigen presenting cell pulsed with an inactivated non-recombinant human immunodeficiency virus (HIV); and a pharmaceutically acceptable carrier." Moreover, claim 55 recites that a *non-anti-retroviral* amount of indinavir is used. Lu would not motivate one of ordinary skill in the art to use a non-anti-retroviral amount of indinavir as recited in that claim.

Lieberman generally discloses that viral mutation of the epitopic sequence recognized by HIV-specific CTL can sidestep CTL recognition. The rejection cites Lieberman for the proposition that it would have been obvious to one skilled in the art to use autologous HIV.

However, Lieberman also fails to disclose "a pharmaceutical composition comprising a therapeutically effective amount of an antigen presenting cell pulsed with an inactivated non-recombinant human immunodeficiency virus (HIV); and a pharmaceutically acceptable carrier."

Therefore, claims 43 and 44 are patentable over Buseyne in hypothetical combination with Lu or Lieberman since they do not teach all the claim limitations whether taken individually or in combination. Claims 51-56 are also patentable over Buseyne combined with Lu or Lieberman because they depend from Claim 43, and recite additional patentable subject matter.

Moreover, the Applicants respectfully submit that the rejection applies an improper "obvious to try" rationale. As noted by the Federal Circuit, "the admonition that 'obvious to try' is not the standard under §103 has been directed mainly at two kinds of error.... what was 'obvious to try' was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general approach guidance as to the particular form of the claimed invention or how to achieve it" *In re O'Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988). Accordingly, even if one of ordinary skill in the art were to combine Buseyne with Lu or Lieberman, there would be no reasonable expectation of success, as required by MPEP 2143.02. Buseyne simply describes that *in vitro* exposure of primary human dendritic cells to AT-2 inactivated HIV strain induces IFN-γ production. Buseyne provides no evidence that the AT-2 inactivated HIV would be effective in an *in vivo* setting. The Examiner's suggestion of the combination is using impermissible hindsight which is based on the Applicants' disclosure, not the prior art.

In view of the foregoing, Buseyne combined with Lu or Lieberman do not support a *prima facie* case of obviousness. The grounds for this rejection have been obviated and withdrawal of the 35 U.S.C. §103 rejection is respectfully requested.

Claims 43-47 and 51-56 stand rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 11/138171 in view of Buseyne, Lu and Lieberman for the reasons set forth on pages 15-21 of the Office Action. The Applicants will address this rejection upon allowance of claims 43-47 and 51-56 of this application, or claim 1 of copending Application No. 11/138171.

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. The Applicants therefore respectfully requests that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. It is believed that a full and complete response has been made to the outstanding Office Action and, as such, the application is in condition for allowance, which is respectfully requested.

Respectfully submitted,

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